LISTING OF THE CLAIMS

1. (Currently Amended) A computer implemented method for predicting [[the]] a three-dimensional structure of a G-protein coupled receptor having a plurality of α helical regions, the method comprising:

identifying ranges of amino acids in an amino acid sequence of the G-protein coupled receptor as transmembrane regions of the G-protein coupled receptor;

constructing each of two or more helices in a set of helices for the transmembrane regions;

obtaining an optimized structure for each of the two or more helices;

assembling the optimized structures of the two or more helices into a helix bundle configuration;

optimizing the helix bundle configuration with a lipid bilayer using a first molecular dynamics simulation;

after optimizing the helix bundle configuration, constructing one or more inter-helical loops to generate a full-atom model of the G-protein coupled receptor;

optimizing the full-atom model using a second molecular dynamics simulation; and

outputting a predicted structure for the G-protein coupled receptor.

2. (Cancelled).

3. (Previously Presented) The method of claim 1, wherein the two or more helices in the set of helices for the transmembrane regions are each canonical right-handed α-helices.

4 – 34. (Cancelled)

35. (Previously Presented) The method of claim 1, wherein the optimizing the helix bundle configuration includes:

calculating a minimum-energy configuration for the helix bundle in the lipid bilayer.

36. (Cancelled)

37. (Previously Presented) The method of claim 1, wherein:
identifying ranges of amino acids in the amino acid sequence as transmembrane regions includes aligning the amino acid sequence with an experimental or theoretical helical template.

38. (Previously Presented) The method of claim 1, wherein identifying a range of amino acids in the amino acid sequence as transmembrane regions includes:
determining the periodicity of hydrophobic residues in the amino acid sequence; and
identifying a plurality of lipid-accessible residues based at least in part on the determined periodicity.

39. (Previously Presented) The method of claim 1, wherein:
obtaining an optimized structure for each of the two or more helices in a set of helices for the transmembrane regions includes optimizing each of the two or more helices using a torsional molecular dynamics method.

40. (Previously Presented) The method of claim 39, wherein:
the torsional molecular dynamics method uses the Newton-Euler Inverse Mass Operator.

41. (Previously Presented) The method of claim 1, wherein:
obtaining an optimized structure for each of the two or more helices includes determining 3-D coordinates for each of the two or more helices.

42. (Previously Presented) The method of claim 1, wherein:
assembling the optimized structures of the two or more helices into a helix bundle includes determining a rotation and tilt of each helix in the set of helices.

43. (Previously Presented) The method of claim 1, wherein:
assembling the optimized structures of the two or more helices into a helix bundle includes orienting axes of the two or more helices according to the 7.5 Å electron density map for rhodopsin.

44. (Previously Presented) The method of claim 38, wherein:
assembling the optimized structures of the two or more helices into a helix bundle includes orienting the identified lipid-accessible residues to face the outside of the helix bundle.

45. (Previously Presented) The method of claim 1, wherein:
the first molecular dynamics simulation is a rigid body molecular dynamics simulation.

46. (Previously Presented) The method of claim 1, wherein:
assembling the optimized structures of the two or more helices into a helix bundle configuration includes modeling an effect of an environment of the membrane-bound protein with a continuum description of a water environment and the lipid bilayer.

47. (Previously Presented) The method of claim 45, wherein:
the first molecular dynamics simulation uses a DREIDING force field, charges derived from charge equilibriation to simulate lipids in the membrane, and charges from CHARMM22 for the G-protein coupled receptor.

48. (Previously Presented) The method of claim 47, wherein:
the second molecular dynamics simulation is a mixed mode molecular dynamics simulation.

49. (Previously Presented) The method of claim 48, wherein the mixed mode molecular dynamics includes:
modeling the helices and inter-helical loops with a torsional molecular dynamics method;

treating lipids in the membrane as rigid bodies, and counterions Na^+ and Cl^- as free Cartesian atoms;

simulating the outside of the lipids with surface-generalized Born model continuum solvent description;

performing constant temperature dynamics with Hoover algorithm for 50 ps with time steps of 1 and 5 fs; and

using a dielectric constant of 60.0 to simulate the low dielectric region surrounding the membrane.

50. (Previously Presented) The method of claim 1, wherein the second molecular dynamics simulation includes:

dynamic optimization of the structure using cell multipole methods for calculation of nonbond forces, and

fast torsional dynamic methods selected from Newton-Euler Inverse Mass Operator and Hierarchical Newton-Euler Inverse Mass Operator.

51. (Previously Presented) The method of claim 1, wherein:

at least the second molecular dynamics simulation includes a solvent approximation.

52. (Previously Presented) The method of claim 51, wherein:

the solvent approximation is a continuum solvation model.

53. (Previously Presented) The method of claim 52, wherein:

the solvent approximation includes the Surface Generalized Born model or the Poisson-Boltzmann description.

54. (Previously Presented) The method of claim 53, wherein:

the solvent approximation is an empirical approximation comprising estimating solvation free energy as a function of solvent accessible protein surface area.

55. (Previously Presented) The method of claim 1, wherein:
the second molecular dynamics simulation is performed for a time in the range from about 100 ps to about 1 ns.

56. (Previously Presented) The method of claim 1, wherein:
the set of helices includes four or more membrane-spanning α-helices.

57. (Previously Presented) The method of claim 1, wherein:
the set of helices includes seven membrane-spanning α-helices.

58. (Cancelled)

59. (Previously Presented) The method of claim 1, wherein the optimizing the full-atom model further includes:
prior to the second molecular dynamics simulation,
performing a full atom minimization of the full-atom model with a barrel of lipid surrounding the protein.

60. (Previously Presented) The method of claim 1, wherein the amino acid sequence of the G-protein coupled receptor is obtained from GeneBank.

61. (Previously Presented) The method of claim 1, wherein the predicted structure is output in protein data bank format.

62. (Previously Presented) A programmable digital computer, configured to perform the method of claim 1.

63. (Previously Presented) A computer program product tangibly embodied in a machine-readable storage device, wherein the computer program includes instructions for executing the method of claim 1 on a programmable processor.

64. (Previously Presented) The method of claim 45, wherein the rigid body dynamics is carried out for 150 ps.